



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,966	12/14/2004	Brian Daniel Doan	PU4754USW	3771
23347	7590	08/23/2007		
GLAXOSMITHKLINE CORPORATE INTELLECTUAL PROPERTY, MAI B475 FIVE MOORE DR., PO BOX 13398 RESEARCH TRIANGLE PARK, NC 27709-3398			EXAMINER CHANDRAKUMAR, NIZAL S	
			ART UNIT 1625	PAPER NUMBER
			MAIL DATE 08/23/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/517,966	Applicant(s) DOAN ET AL.	
	Examiner Nizal S. Chandrakumar	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-29 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____ |

Art Unit: 1625

DETAILED ACTION

This application filed 12/14/2004 is a 371 of PCT/US03/20094 06/25/2003 which claims benefit of 60/392,677

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 15-19 of copending Application No. 10/560500. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the instant claims is part of the claimed subject matter of the copending application. Further the copending application describes the preparation as well as the enzymatic resolution of compounds of the instant case (the compounds are shown below as A and B, under *Claim Rejections - 35 USC § 112*). See page 15, Examples 3-7 of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 12 of U.S. Patent No. 7145024. Although the conflicting claims are not

Art Unit: 1625

identical, they are not patentably distinct from each other because the resolution of hexahydrofuro[2,3-b]furan-3-ol compound of the instant case is the subject matter of the claim 12 of the issued patent.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,3,4,6,13,16-17 are rejected under 35 U.S.C. 112, second paragraph, as being vague and indefinite.

In claims 1, 3 it is unclear what C6-14 aryl means; what are the aryl groups other than C6, C10 or C14?

Enzymatic resolutions are performed on esters. Claim 3 omits the esterification step, such as the use of vinyl acetate. Likewise the claims 4, 6, 11 are missing many reaction steps.

In claim 6, the term 'substantially free' is vague and indefinite. It is suggested that the expression is substituted in accordance with the definition on page 9.

The formula (XIX) of claim 13 is not in line with the same on pages 11-12 of the specification. The terms 'optionally resolving' in claim 13 imply that the reaction is enantio- and stereo- specific. Based on the specification this is not the case. Appropriate correction is required. Further, the reagents specified in step b) are not in line with the compound of formula (XIX); or there is a step missing for the conversion of other halogens to bromine of the formula (XIX).

Claims 16 and 17 are the same.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

Art Unit: 1625

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-6, 11, 13, 15, 18-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some of the reagents, does not reasonably provide enablement for the wide variety of reagents claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims recite numerous possible reagents but the disclosure in the specification is not sufficient to support all these reagents. For instance, NBS is the only reagent that is enabled in the specification for the halo-cyclization.

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the relevant factual considerations.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)).

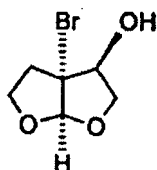
- 1) The breadth of the claims,
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

While all the above factors were considered, some of the specific considerations are described below:

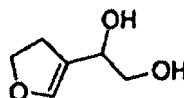
The nature of the invention: The claims are drawn to the process of making bicyclic hexahydrofuro[2,3-b]furan-3-ol compounds such as (A) optionally substituted at the 3-position with halogens, in which

Art Unit: 1625

compound (B) is the precursor to A.



Br is A



B

The breadth of the claims: The claims recite a wide variety of reagents that could effect the cyclization of B to form A. The claims also recite lipase-mediated resolution of ester-substrates in which the esters are derived from carboxylic acids of wide structural variation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the art of organic synthesis, it is noted that each embodiment of the invention is required to be individually assessed for viability.

The amount of direction or guidance present: The specification contains many theoretical possibilities of resolution and separation schemes that are available for making compounds with des and ees in excess of 90%. For example the specification indicates on page 4 (Scheme B, line 2) that a diastereomeric mixture 'can be' separated by 'extraction'. It is not clear how this selective extraction of very similar compounds can be accomplished. It is unclear, if 'the selective extraction' relates to subsequent resolution.

The existence of working examples: The specification contains direction for making compounds in which the halo-cyclization could be performed with one reagent. I.e., NBS. The specification contains direction for the resolution of enantiomers (and diastereomeric mixtures) for the acetate derivatives of the cyclized compounds, i.e., R₂ = CH₃.

Art Unit: 1625

The state and the predictability of the art: The prior art is unpredictable as to the nature of the cyclization. There is no description in the specification regarding the mechanistic aspect of the halocyclization. For instance, it is not clear whether a bromonium ion (5-endo-tet) or an oxonium (5-exo-trig) is the immediate precursor to the cyclization or any other mechanism operating that could enable the use of the many reagents (positive halogen sources) claimed.

The state of the art is unpredictable with respect to the resolution of prochiral esters. Given that the resolution is enzymatic, the structure of ester substrate is of major significance with respect to the outcome of any resolution experiment. For instance, the extent of resolution (ee) of the ester of the alcohol derived from acetic acid and phenanthrene-1-carboxylic acid would be different when the same lipase is used.

The quantity of experimentation needed: In the instant case, there is a substantial gap between the processes demonstrated and the breadth of the claims. Given the direction and working Examples provided in the specification, in order to utilize the invention as claimed, the skilled artisan would be presented with an unpredictable amount of experimentation. The guidance provided in the specification limits the number of possible reagents useful for the halo-cyclization to one, i.e. NBS. The guidance provided in the specification limits the number of possible ester substrate useful for resolution to one, i.e. acetates. The instant disclosure is broad and generic.

Enablement is provided in the specification for halocyclization using NBS; i.e. for halo-compounds made, the halogen is Br.

Enablement is provided in the specification for resolution of acetates of the bicyclic alcohols, i.e., the lipase mediated resolution substrates are acetates.

No claims are allowed.

Art Unit: 1625

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nizal S. Chandrakumar whose telephone number is 571-272-6202. The examiner can normally be reached on 8.30 am – 5 pm Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at 571-272-0867 or Primary Examiner D. Margaret Seaman can be reached at 571-272-0694. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Nizal S. Chandrakumar


D. MARGARET SEAMAN
PRIMARY EXAMINER